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EDITORIAL

Genome editing for dissecting and curing human genetic diseases

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Genetic disorders in humans are caused by various types of genomic aberrations, such as point mutations, insertions and/or deletions, and chromosomal rearrangements including inversions and translocations. It had been highly unlikely that these errors in genomic DNA could directly and precisely be reproduced or corrected in human cells and in animal organisms, prior to the emergence of genome editing technology. Recently, functional genomics studies have been highly accelerated by this rapidly evolving technology. Genome editing depends on a site-specific introduction of DNA double-strand break (DSB), followed by error-prone or exogenous donor-dependent DSB repair, resulting in gene knockout or knock-in, respectively. The basic system of genome editing was established in 1990s, but the technology became explosively grown and sophisticated in 2010s.

The driving force of such technological burst was the development of CRISPR-Cas9 system, which possessed robust activity of DSB introduction and enabled easy construction of nuclease tools. Initially developed nuclease, SpCas9 (Cas9 from *Streptococcus pyogenes*), had several limitations such as large protein size, restriction of targetable sequence depending on protospacer adjacent motif, and relatively high risk of off-target mutations; however, these limitations have quickly been overcome in various ways, including protein engineering of SpCas9, and discovering and characterizing Cas9 from other bacterial species or other types of Cas proteins such as Cpf1. Along with the development of nuclease tools, various applied systems have also been developed in a rapid pace. For example, gene knock-in has currently been applied not only through homologous recombination but also through various kinds of DSB repair pathways including non-homologous end-joining and microhomology-mediated end-joining. Combined applications of genome editing tools and mammalian artificial chromosome vectors have opened up a new avenue of megabase-sized introduction or replacement of genomic regions. Genome-wide CRISPR screening systems have enabled forward genetics studies in human cells. Scarless control of gene function has been achieved by the transcriptional activation/repression systems via artificial transcription factor and epigenome editing systems.

In this special issue, recent advances on genome editing technologies for dissecting and curing human genetic diseases are summarized in nine review articles. These include current status of genome editing in various mammalian species such as mice, rats, and marmosets, genome editing in cultured cells, in stem cells, and *in vivo*, and various expanded applications, such as chromosome transfer-mediated disease modeling and humanization, CRISPR screening, and epigenome editing. We believe our special issue serves as a comprehensive guide to the front-line of genome editing technology for mammalian genetics studies.

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